Early Pars Plana Vitrectomy for Treatment of Acute Infective Endophthalmitis

I-Van Ho, PhD, FRANZCO,† Guillermo Fernandez-Sanz, MD, DiSSO,*‡ Steve Levasseur, MD, FRCSC,* Eugene Ting, MBBS,*† Gerald Liew, PhD, FRANZCO,†§ Justin Playfair, MBBS(Hons), FRANZCO,*† John Downie, MBBS(Hons), FRANZCO,*¶ Mark Gorbatov, MBBS(Hons), FRANZCO,* Alex P Hunyor, MBBS(Hons), FRANZCO,*† and Andrew A Chang, PhD, FRANZCO*||*

Purpose: To evaluate the efficacy and safety of early pars plana vitrectomy (PPV) for the treatment of acute infective endophthalmitis, and identify prognostic factors for better visual outcome.

Design: Retrospective cohort study.

Methods: Consecutive patients who underwent early PPV within 72 hours of presentation for the treatment of acute infective bacterial endophthalmitis and presented to a large tertiary referral center in New South Wales, Australia, between January 2009 and December 2013 were included. Changes in best-corrected visual acuity (VA) from baseline to 1 year were examined.

Results: A total of 64 patients were included. The inciting events were cataract surgery (53%), intravitreal injection (36%), trabeculectomy (3%), and endogenous (3%). The mean VA improved from 3.1 logMAR (hand motion) at baseline to 1.02 (approximately 20/200) at 1 year, with 42% achieving final VA equal to or better than 0.477 logMAR (20/60) following early PPV. Positive prognostic factors were negative microbial cultures ($P < 0.01$) and etiology of post–cataract surgery ($P < 0.01$). In multivariable analyses adjusting for age and prognostic factors, patients with baseline VA of light perception and hand motion achieved greater visual gains than those with counting fingers, with gains of logMAR of −2.68, −2.09, and −0.85, respectively ($P < 0.0001$).

Conclusion: Most patients who undergo early PPV experience substantial VA improvement. Negative microbial cultures and endophthalmitis after cataract surgery were associated with better final visual outcome. Patients with presenting VA of light perception or hand motion achieved higher visual gains than those with counting fingers, suggesting the possibility that early PPV may be beneficial in both groups.

Key Words: cataract surgery, early vitrectomy, endophthalmitis, intravitreal injection, visual acuity

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Acute-onset infectious endophthalmitis (IE) remains one of the most challenging and devastating complications in ophthalmic surgery. It is defined as severe inflammation of the ocular tissues and fluids resulting from either direct inoculation of a pathogen from surgery or trauma, or from the hematogenous spread of organisms from a distant source.[1]

Since 1995, management of acute-onset IE has been based predominantly on findings of the Endophthalmitis Vitrectomy Study (EVS).[1] This prospective randomized trial found no benefit from immediate pars plana vitrectomy (PPV) when compared with vitreous tap and intravitreal injection of antibiotics in patients with IE after cataract surgery, except in the subgroup where visual acuity (VA) at presentation was light perception (LP) or worse. More recently, there have been suggestions that PPV should be performed earlier and in patients with better than LP vision.[2–5] It is thought that early vitrectomy may be beneficial as it allows for the debridement of bacteria, inflammatory cells, and other toxic debris from the vitreous cavity; promotes better diffusion of antibiotics; removes inflammatory membranes and provides earlier visualisation of the retina.[1] Significant advancements in vitreoretinal surgery technology have occurred since the EVS was published.[6,7] This has allowed surgeons to perform a more thorough vitrectomy while reducing the risk of inducing iatrogenic retinal injury and subsequent retinal detachment.

Moreover, the patient population presenting with acute IE postoperatively is evolving with the increasing number of cases due to intravitreal injections.[5,8–11] The direct inoculation of infectious pathogens into the vitreous cavity and the higher frequency of *Streptococcus* spp associated with this patient population makes it different from IE after cataract extraction.[12–14] These factors point to the need for more data on early PPV for acute IE to guide the optimal management of contemporary patients.

The purpose of this study was to evaluate the efficacy and safety of micro-incisional early PPV for the treatment and management of patients presenting with acute-onset IE. We also aimed to identify prognostic factors for better visual outcome in this patient population.

METHODS

We performed a retrospective cohort study of 64 consecutive patients who underwent early PPV within 72 hours of presentation for the treatment of acute-onset IE. The charts of all patients who presented to the Sydney Eye Hospital, a tertiary referral center for the state of New South Wales, Australia, with suspected acute-onset IE and underwent early PPV between January 2009 and December 2013 were reviewed. Inclusion criteria were a clinical diagnosis of microbial endophthalmitis confirmed by a vitreoretinal specialist, documented anterior-chamber hypopyon

From the *Retina Unit, Sydney Eye Hospital, Sydney, NSW, Australia; †Retina Associates, Sydney, NSW, Australia; ‡Clinica Universidad de Navarra, Madrid, Spain; §Westmead Institute of Medical Research, University of Sydney, NSW, Australia; ¶Sydney Retina Clinic and Day Surgery, Sydney, NSW, Australia; and ||Retina Consultants, Sydney, NSW, Australia.

I.H., G.F., and S.L. contributed equally to this work and are considered co-first authors.

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Reprints: I-Van Ho, Sydney Eye Hospital, 8 Macquarie St, Sydney NSW 2000, Australia. E-mail: ivanho1973@hotmail.com.

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and fibrin, loss of red reflex, and vitreous opacities present on B-scan ultrasound. All cases had a minimum of 12 months' follow-up after the initial surgery. Approval was obtained from the South East Sydney Local Health District Human Ethics Review Board for this study. Because this retrospective study was carried out using patient data in an anonymous manner, the requirement for written informed consent from individual patients was waived.

Data collected from clinical records included: age; sex; ocular history; cause of endophthalmitis; number of days from inciting event to presentation; number of days from presentation to undergoing PPV; Snellen best-corrected VA at presentation and 1, 3, 6, and 12 months postoperatively, as well as at the last follow-up visit. The presenting symptoms and findings, intraoperative techniques, culture results, complications (retinal detachment, epiretinal membrane, ocular hypotony or hypertension, phthisis, and evisceration), and length of follow-up were also documented. Visual acuities were converted to logMAR values, as per the description by Ferris et al.[15] A logMAR of +4.0, +3.0, and +2.0 was assigned to VA of LP, hand motion (HM), and counting fingers (CF) vision, respectively, according to the methods published by Holladay.[16]

The indication for early PPV in this study was poor vision (CF or worse) at presentation. All patients in this study underwent a standard pars plana vitreous tap and injection protocol at presentation prior to undergoing PPV. An initial preparation with a drop of anesthetic (0.5% tetracaine) and povidone-iodine solution was applied to the affected eye. Subconjunctival lidocaine (2%) was injected near the anticipated site of intravitreal injection. Sterile preparation of eyelashes and eyelids with povidone-iodine was performed. A 0.2-mL vitreous sample was taken for microbiological assessment followed by intravitreal injection of 1 mg of vancomycin in 0.1-mL solution and 2.25 mg of ceftazidime in 0.1-mL solution.

All patients subsequently underwent standard 23-gauge 3-port PPV within 72 hours of presentation. Anterior chamber washout was performed in all patients. A core vitrectomy was undertaken and the amount of vitreous removed was directly related to quality of the surgical view. When required, the corneal epithelium was debrided. If a retinal break or retinal detachment was seen intraoperatively, endolaser and/or cryoretinopexy was applied to the affected area. Silicone oil was used as an endotamponade agent in all cases when retinal detachment was present intraoperatively. In the remaining cases, a partial fluid-air exchange followed by intravitreal injection of 1 mg of vancomycin and 2.25 mg of ceftazidime was performed. Postoperatively, all patients were treated with topical antibiotics and steroids as well as oral ciprofloxacin.

The primary outcome of this study was final VA at 1 year. The secondary outcomes were adverse events associated with surgical intervention as well as prognostic factors associated with improvement in final VA.

Statistical Analysis

We compared categorical variables using Fisher exact test, and continuous variables using the paired samples *t* test. Multivariable mixed models were constructed using variables that were associated with improvement in final VA in univariable analyses. All analyses were performed with SAS software, version 9.4 (SAS Institute, Cary, NC, US). A *P* value of <0.05 was considered statistically significant.

RESULTS

A total of 64 eyes of 64 patients (36 women and 28 men) met the inclusion criteria during the 5-year study period. The median age was 77.5 years (range, 43–92 years) at the time of surgery (Table 1). The inciting factor for IE was phacoemulsification and intraocular lens implant in 34 patients (53%), intravitreal injections in 23 patients (36%), trabeculectomy surgery in 2 patients (3%), endogenous source in 2 patients (3%), and the remaining 3 (5%) followed a vitrectomy, an intraocular lens exchange, and a globe rupture (Table 1). Of 23 patients secondary to intravitreal injections, 19 (83%) were post ranibizumab, 2 (9%) post triamcinolone, 1 (4%) post bevacizumab, and 1 (4%) post aflibercept. The mean time of onset from the inciting factor, excluding the 2 endogenous cases, was 5.7 days. The interval between injection and subsequent vitrectomy was within 72 hours. The mean time from antibiotic injection to undergoing vitrectomy was 0.8 days. The decision was based on clinical evidence of worsening. The 2 patients who developed endophthalmitis after intravitreal triamcinolone had culture-positive vitreous taps, which grew *Staphylococcus epidermidis* and *Staphylococcus aureus*. Of the 42 (66%) culture-positive samples, 43% grew *S. epidermidis*; 33% grew *Streptococcus* spp; 12% grew *S. aureus*; 5% grew *Enterococcus* spp; and 2% grew *Haemophilus*, *Klebsiella*, and *Moraxella* spp (Table 1).

Table 2 summarizes the mean VA endpoints for all patients

TABLE 1. Baseline Characteristics of Patients with Endophthalmitis (n = 64)

	No. (%) of Patients*
Demographics	
Age, y	
Mean ± SD	74.8 ± 11.4
Median; range	77.5; 43–92
Sex	
Female	36 (56)
Male	28 (44)
Eyes	
Right	27 (42)
Left	37 (58)
Etiology	
Phacoemulsification	34 (53)
Intravitreal injection	23 (36)
Other	7 (11)
Time of onset (excluding endogenous), d	
Mean ± SD	5.7 ± 9.5
Median; range	4; 2–77
Time from injection to vitrectomy, d	
Mean ± SD	0.8 ± 1.2
Median; range	0 (same day); 0–3
Culture positive	42 (66)
Gram-positive	39 (93)
Staphylococcus epidermidis	18 (43)
Staphylococcus aureus	5 (12)
Enterococcus spp	2 (5)
Streptococcus spp	14 (33)
Gram-negative	3 (7)

*Unless otherwise stated.

as well as the subgroups of patients based on culture results, type of microorganism, as well as inciting factor at presentation, 1 month, 3 months, 6 months, and 1 year (mean follow-up, 21.9 weeks). Considering all patients enrolled, the presenting mean VA was logMAR of +3.1 which improved to +1.02 at 1 year ($P < 0.001$). Presenting VA was worse for patients who were culture positive than culture negative (logMAR, +3.26 vs +2.79; $P = 0.03$), but similar for cataract surgery and intravitreal injection patients (logMAR, +3.06 vs +3.07, $P = 0.96$). Most patients experienced substantial improvement in VA, with 57 patients (89%) improved by 1 line or greater.

Univariate and multivariate analyses were performed to identify predictive factors for improvement in VA (Table 3). The group with the highest proportion of patients with VA equal to or better than +0.3 logMAR were those with culture-negative results (45% of patients), compared with 14% of patients with culture-positive results. Of those that were gram-positive, only patients who grew *S. epidermidis* had a VA equal to or better than +0.3 logMAR (33%, $P = 0.04$); patients with other gram-positive organisms had poorer outcomes.

Table 3 also shows that patients who developed IE after cataract surgery had better outcomes compared with those who had intravitreal injections. At 1-year post diagnosis, 35% of patients who had cataract surgery had a VA equal to or less than +0.3 logMAR compared with 13% of patients who had intravitreal injections, although the difference was not statistically significant

TABLE 2. Changes in Visual Acuity After Early Vitrectomy from Baseline to 1 Year

	Mean (Median) Visual Acuity (logMAR)									
	At Baseline	***P* value***	**At 1 Month**	***P* value***	**At 3 Months**	***P* value***	**At 6 Months**	***P* value***	**At 1 Year**	***P* value***
All patients	3.1 (3)		1.44 (1)		1.08 (1)		1.02 (0.89)		1.02 (0.89)	<0.001
Culture-positive	3.26	0.03	1.66	0.02	1.32	0.005	1.26	0.003	1.22	0.01
Culture-negative	2.79		0.99		0.64 (4)		0.58		0.65	
Gram-positive	3.31 (3)	0.11	1.59 (1.3)	0.08	1.28 (1)	0.27	1.21 (1)	0.22	1.18 (1)	0.19
Gram-negative	2.67 (3)		2.67 (3)		2 (2)		2 (2)		2 (2)	
Staphylococcus epidermidis	3.11 (3)	0.18	1.30 (1)	0.34	0.99 (0.54)	0.17	0.88 (0.48)	0.11	0.86 (0.48)	0.11
Staphylococcus aureus	3.6 (4)		1.98 (2)		1.77 (2)		1.77 (2)		1.74 (2)	
Streptococcus spp	3.36 (3.5)		1.84 (2)		1.53 (1.3)		1.46 (1.3)		1.39 (1.3)	
Enterococcus spp	4 (4)		1.5 (1.5)		1 (1)		1 (1)		1 (1)	
Cataract surgery	3.06 (3)	0.96†	1.08 (0.6)	0.04†	0.74 (0.48)	0.002†	0.70 (0.48)	0.0009†	0.73 (0.48)	0.002†
Intravitreal injection	3.07 (3)		1.80 (2)		1.51 (1.3)		1.46 (1.3)		1.42 (1.3)	
Other‡	3.43 (4)	0.38	2 (2)	0.22	1.31 (1)	0.83	1.04 (0.77)	0.74	1.02 (0.7)	0.66

*Calculated using Student T test or analysis of variance, compared with baseline.

†Comparing cataract surgery with intravitreal injection.

‡Other refers to trabeculectomy/intraocular lens exchange/vitrectomy/globe rupture/endogenous endophthalmitis; *P* values are compared with cataract surgery.

TABLE 3. Visual Acuity of Patients 1 Year Post Early Vitrectomy

	logMAR Visual Acuity with Snellen Equivalent, No./Total (%) of Patients							
	≤0.3 20/40	***P* value***	**≤0.477 20/60**	***P* value***	**≤0.7 20/80**	***P* value***	**>1.6 20/800**	***P* value***
All patients	16/64 (25)		27/64 (42)		32/64 (50)		15/64 (23)	
Culture-positive	6/42 (14)	0.006	11/42 (26)	0.0005	15/42 (36)	0.003	12/42 (29)	0.23
Culture-negative	10/22 (45)		16/22 (73)		17/22 (77)		3/22 (14)	
Gram-positive	6/39 (15)	0.46	11/39 (28)	0.55	15/39 (38)	0.25	10/39 (26)	0.19
Gram-negative	0		0		0		2/3 (67)	
Staphylococcus epidermidis	6/18 (33)	0.04	10/18 (56)	0.002	12/18 (67)	0.001	4/18 (22)	0.25
Staphylococcus aureus	0		1/5 (20)		1/5 (20)		3/5 (60)	
Streptococcus spp	0		0		1/14 (7)		3/14 (21)	
Enterococcus spp	0		0		0		1/2 (50)	
Cataract surgery	12/34 (35)	0.06	18/34 (53)	0.04	21/34 (62)	0.05	5/34 (15)	0.11
Intravitreal injection	3/23 (13)		6/23 (26)		8/23 (35)		8/23 (35)	
Cataract surgery	12/34 (35)	0.37	18/34 (53)	0.99	21/34 (62)	0.67	5/34 (15)	0.28
Other†	1/6 (17)		3/6 (50)		3/6 (50)		2/6 (33)	

*Calculated using Chi square or Fisher exact test (if <5 counts in any cell).

†Other refers to trabeculectomy/intraocular lens exchange/vitrectomy/globe rupture/endogenous endophthalmitis.

($P = 0.06$). Similarly, post–cataract surgery patients had a greater likelihood of achieving a logMAR of +0.477 ($P = 0.04$) and +0.7 ($P = 0.05$) or better when compared with those who had intravitreal injections.

Table 4 shows the results of the multivariate analyses. Only presenting VA and sex were independently associated with improvements in VA from baseline to 1 year. Patients with VA of LP or HM at presentation gained substantially more vision than those with CF. Men gained more vision than women at 1 year.

Intraoperative and postoperative complications were relatively common. Of 64 patients, 6 (9%) had intraoperative rhegmatogenous retinal detachment; 4 of them were diagnosed preoperatively with B-scan ultrasound. There were 4 patients (6%) who had retinal detachment postoperatively, occurring at a median time of 11 days (SD, 23; range, 7–56 days) after surgery. Two patients (3%) required an evisceration, of whom both had intraoperative retinal detachment. Six patients (9%) developed epiretinal membrane, 1 (2%) had postoperative hypotony and 4 (6%) developed ocular hypertension. Of the latter 4 patients, 3 still required topical hypotensive agents at the last follow-up examination. Among the patients who developed retinal detachment, final VA at 1 year was 1.9 (slightly better than CF). All had silicone oil removed by that time.

DISCUSSION

In this retrospective cohort study of patients who underwent early PPV for IE, a majority experienced some degree of visual recovery. A total of 89% of patients experienced visual improvement of 1 line or better while only 3% had worse vision at 1 year. Cataract surgery as the etiological cause and negative microbial cultures were positive prognostic factors, and in multivariable analyses patients with LP- or HM-baseline VA achieved more visual gains after early PPV than those with CF vision.

There is controversy regarding the role of early PPV in treating IE.[2,17–19] Chaudhary et al[11] found that patients underwent tap and injection of intravitreal antibiotics alone regained baseline VA more often than those who underwent tap and injection with subsequent PPV (90% vs 46%). Kurniawan et al[20] and Xu et al[21] have also reported no benefit of early PPV in improving visual outcomes. Population studies in the US and Australia have reported that PPV usage is higher than that recommended by the EVS, but with no evidence of increased benefit.[3,22]

In contrast, a number of case series have reported good outcomes following early PPV. Panarci et al[23] reported 40% of their patients achieved final VA of 20/40, while other studies by Kuhn and Gini,[4] Tan et al,[24] and Almanjoumi et al[25] have reported even higher percentages of 91%, 83.3%, and approximately 80% achieving final VA of 20/40, respectively. Another retrospective study found only early PPV was associated with better visual outcome in streptococcal IE.[26] Finally, surveys of ophthalmologists have found the majority perform early PPV if there is clinical worsening within 48 hours following tap and injection of antibiotics.[27] In our study, 23% of patients achieved a final VA of 20/40 following early PPV, which is lower than that reported in other series (40%–91%).[4,23–25] This may be due to the relatively high percentage of patients with preexisting poor visual potential due to macular degeneration and who were receiving intravitreal anti–vascular endothelial growth factor therapy in our study.

We identified post–cataract surgery etiology and culture-negative microbial growth as positive prognostic factors for better final VA. These factors have also been identified in other studies.[28,29] Culture-positive cases may indicate more virulent bacteria as well as the presence of a greater intraocular bacterial load. Of those cases that were culture positive, *S. epidermidis* was associated with a better visual outcome compared with other pathogens, which has also been reported by others.[28,29] In multivariable analyses adjusting for age, sex, culture, etiology, days from surgery and baseline vision, poorer baseline vision was most strongly associated with improvement in VA, with a weaker association of male sex. This suggests that while surgical etiology and culture results are predictive factors for VA improvement following early PPV, their prognostic value is captured in baseline VA measurements. This finding reveals the importance of measuring baseline VA and validates the EVS approach of determining treatment based on baseline vision.[1] Further, we report that patients with baseline VA of LP or HM experienced similar visual gains, suggesting that early PPV may be beneficial not only for patients with presenting VA of LP (as shown by the EVS), but also for patients with HM vision. A randomized clinical trial of early PPV is warranted in this area.

Strengths of this study include a moderately large sample size, inclusion of multiple etiologies including post–cataract surgery and intravitreal injections, recruitment from a single center with less variability in PPV protocols, and adjustment for predictive factors including baseline VA. Limitations include the retrospective nature of data collection and lack of a control

TABLE 4. Multivariate Analyses of Variables Predicting the Change in Visual Acuity After Early Vitrectomy

Variable	Change (SD) in logMAR Visual Acuity* Baseline to 1 Year	*P* value
Age, y		0.71
≤78	−2.05 (1.02)	
>78	−2.09 (1.06)	
Sex		0.03
Female	−1.88 (1.03)	
Male	−2.31 (1.00)	
Culture		0.12
Negative	−2.14 (1.15)	
Positive	−2.03 (0.98)	
Etiology		0.11
Intravitreal injection	−1.64 (1.04)	
Other	−2.48 (0.96)	
Cataract surgery	−2.29 (0.97)	
Days from initial surgery		0.62
≤4	−2.23 (1.02)	
>4	−1.85 (1.02)	
Baseline visual acuity, logMAR		<0.0001
+4.0 (light perception)	−2.68 (0.91)	
+3.0 (hand motion)	−2.09 (0.84)	
+2.0 (counting fingers)	−0.85 (0.78)	

*Adjusted for age, sex, culture, etiology, days from surgery, and baseline vision.

group. We did not include a control group such as patients who received only a tap and injection of antibiotics as these patients have milder forms of IE with better prognosis, and comparison with the more severe patients with early PPV would introduce confounding by indication. This bias can only be fully dealt with in a randomized controlled trial setting.

In conclusion, our study showed that a majority of patients with acute IE undergoing early PPV experience VA improvement. Endophthalmitis after cataract surgery and negative microbial cultures predicted better final visual outcome. After adjusting for these and other factors, patients with presenting VA of LP or HM achieved higher visual gains than those with CF, suggesting early PPV may be beneficial in patients with HM- as well as LP-baseline VA. Since the publication of the EVS, significant changes in the etiological causes and surgical management options for the treatment of acute IE have occurred, and the indications for early PPV may need to be re-examined, preferably in a new randomized clinical trial.

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